Protocol for Evaluating Safety and Efficacy of a Wildlife Vaccine against Brucellosis in the GYA

Prepared for the Greater Yellowstone Interagency Brucellosis Committee

The purpose of this protocol is to establish guidelines for the development and evaluation of new brucellosis vaccines to be used in free-ranging elk (*Cervus elaphus*) and bison (*Bison bison*) inhabiting the Greater Yellowstone Area. This protocol is not intended to evaluate current vaccination programs being applied to these species. The recommendations for the following criteria regarding efficacy and safety are based on the assumption that any brucellosis vaccine evaluated by these criteria would have defined dosage, route of administration, and age restrictions for any application of the vaccine. The vaccine strain will demonstrate stable characteristics following in vitro and in vivo passage. Efficacy evaluations within the principal species should include animals of minimal recommended age, at the minimally recommended dosage and administered in accordance with recommendations. For safety evaluations within the principal species, animals should be of minimal recommended age, at the maximal recommended dosage, and administered in accordance with recommendations. The assumption is also made that the criteria for approval of a vaccine as safe will be the same in both male and female animals in the targeted population. For the purposes of this paper, the definition of a calf will be a bison or elk of less than 12 months of age. Restrictions on use (e.g., sex, age) may be applied without rejection of the vaccine in total. For example, limit use to females because of adverse reactions in males.

Calfhood Vaccination

Safety

- To be defined as safe, a vaccine would not have any clinical effects that would increase predation or decrease survivability. However, adverse clinical effects, such as listlessness, anorexia, depression, and arthritis, that are transient and minimal with no long-term effects on survival may be acceptable. There should be no statistical difference between vaccinates and controls on these factors.
- A safe calfhood vaccine will not be shed from a vaccinate prior to parturition. The vaccine strain will not persist to the first calving in 95% or greater of the vaccinated individuals, or persistence of the vaccine strain will not be associated with a significant reduction in the survivability (i.e.,. no pathology) or the reproductive potential of the individual (i.e. repeated fetal loss, infected calves, or decreased fertility). There should be no statistical difference between vaccinates and controls on these factors.

Efficacy

- To be defined as efficacious in females, a vaccine must induce statistically greater protection against fetal loss, infected calves, or infection in pregnant vaccinates after experimental challenge when compared to non-vaccinated animals in the same experiment. Infection is defined as either number of colony-forming units (CFU) per gram of tissue and/or number of infected tissues.
- Use of model predictions must indicate that the vaccine, when used alone without other management influence, will reduce the prevalence of brucellosis in the targeted wildlife population.
- Experiments will need to be conducted to evaluate the duration of immunity of the vaccine but these experiments will not be required for initiation of use of the vaccine if all other safety and efficacy criteria are met. A vaccine should provide long-term immunity and/or be able to be safely boosted during the life of the animal.

Adult Vaccination

Safety

- A safe vaccine will not induce significant reductions in survivability or reproductive efficiency as statistically demonstrated in clinical trials.
- A safe vaccine will not cause a significant reduction in recruitment in the population of the target species.

Efficacy

- A vaccine will be determined to be efficacious if it induces statistically greater protection in vaccinates against fetal loss, infected calves, or infection after experimental challenge when compared to non-vaccinated animals in the same experiment. In addition, modeling must indicate that the vaccine, when used alone without other management influence, will reduce the prevalence of brucellosis in the targeted wildlife population.

Other

- A major advantage of any vaccine would be the ability to differentiate vaccinates from animals infected with Brucella field strains either by a serologic test or by alternative methods.

Nontarget Species

A vaccine candidate cannot cause deleterious effects on the short-term survivability of representative ungulates, rodents, carnivores or avian species under experimental conditions. Candidate species that should be strongly considered for evaluation include moose, bighorn sheep, antelope, mule deer, coyotes, wolves, ravens, microtus, peromyscus, and ground squirrels. Other species could be added if scientific data supports their inclusion.

Adopted by the
Greater Yellowstone Interagency Brucellosis Committee
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